REMARKS

A check in the amount of $180 for a Supplemental Information Disclosure Statement is enclosed. Any fees that may be due in connection with the filing of this paper, if the attached check is in the wrong amount, improper or is missing, or with this application during its entire pendency, may be charged to Deposit Account No. 50-1213. If a Petition for an Extension of Time is required, this paper is to be considered such petition.

Claims 5-7, 11-16, 29, 33-37, 39, 45 and 49 are pending herein. Claims 5, 12, 13 and 33 are amended. Basis for the amendments to the claims can be found in the claims as originally filed and in the specification. In particular, the addition of the proviso to claim 6 finds basis in the specification, on page 7, line 12-14, and page 20, lines 27-29, which recite that:

> In other more preferred embodiments, the LPCs are chosen with the proviso that Z contains at least one, preferably at least two, more preferably at least three **or more** phenylene or alkylene units.

Thus, the amendment has basis in the specification and no new matter has been added.

REJECTION OF CLAIMS 5-9, 27-40 and 45-49 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 5-9, 11-16, 29, 33-37, 39, 45 and 49 are rejected under 35 U.S.C. §112 as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed subject matter. The Office Action notes that the claims are directed to liquid phase carriers (LPCs), of formula (Ia) that do not contain 2'-deoxythymidine-3'-O-yl and methods of using the same in solution phase biopolymer synthesis. It is further noted in the Office Action that particular compounds of formula (Ia) that do not contain 2'-deoxythymidine-3'-O-yl, namely tetrakis-{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-

deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ((DMT-dT)$_4$-PE-LPC) and tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT$_4$-PE-LPC), as well as their preparation is described in the specification. The Office Action alleges that the disclosure is not adequate to satisfy the written disclosure for how to make LPCs of formula (Ia) wherein A is silicon. It is further urged that the support in the specification is not adequate for the claim to the method of solution phase biopolymer synthesis using such LPCs of formula (Ia). The Office Action urges that there is no predictability established in the art with respect to synthesizing a substituted silicon compound based on the synthesis of a substituted methane compounds. It is alleged that the data presented in the application shows the synthesis of methane substituted with an amide or diamide, which is not seen to be adequately correlative for the elected species of a silicon based compound substituted with alkyl or phenyl groups as broadly claimed. The Office Action concludes that there is not enough data to support the claim that Applicant had possession of the claimed subject matter at the time of filing. Applicant respectfully disagrees.

Relevant Law

The purpose behind written description requirement is to ensure that the patent applicant had possession of the claimed subject matter at the time of filing of the application In re Wertheim, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). The manner in which the specification meets the requirement is not material; it may be met by either an express or an implicit disclosure.

35 U.S.C. §112 requires a written description of the invention. This requirement is distinct from and not coterminous with the enablement requirement:

> The purpose of the 'written description' requirement is broader than to merely explain how to 'make and use'; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is,

> for purposes of the 'written description' inquiry, whatever is now claimed." Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563-64, 19 USPQ2d at 1117 (emphasis in original).

The issue with respect to 35 U.S.C. §112, first paragraph, adequate written description, has been stated as:

> [d]oes the specification convey clearly to those skilled in the art, to whom it is addressed, in any way, the information that appellants invented that specific compound [claimed embodiment] Vas-Cath, Inc. v. Mahurkar, at 1115, quoting In re Ruschig, 390 F.2d 1990, at 995-996, 154 USPQ 118 at 123 (CCPA 1967).

A specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, *i.e.*, whatever is now claimed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ.2d 1111, 1117 (Fed. Cir. 1991). A written description requirement issue generally involves the question of whether the subject matter of a claim is supported by or conforms to the disclosure of an application as filed. The test for sufficiency of support in a patent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)) (see also, MPEP 2163.02).

An objective standard for determining compliance with the written description requirement is "does the description clearly allow persons of skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ.2d 1614, 1618 (Fed. Cir.1989). The Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. In re Wertheim, 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976); *See also* Ex parte Sorenson, 3 USPQ.2d 1462, 1463 (Bd. Pat.App. & Inter. 1987). By disclosing in a patent application a

device that inherently performs a function or has a property, operates according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter. In re Reynolds, 443 F.2d 384, 170 USPQ 94 (CCPA 1971); and In re Smythe, 480 F. 2d 1376, 178 USPQ 279 (CCPA 1973).

The instant claims

Instant claim 5 is directed to a liquid phase carrier (LPC) of formula (Ia):

$$(R^1)_p\text{-}A\text{-}(Z\text{-}X^1)_n \quad \text{(Ia)}$$

where:

A is silicon;

n is 3 or 4; and

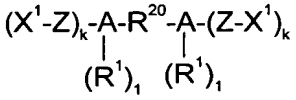
the remaining variables are as defined therein.

Claims 6, 7 and 11-16 further define the variables in claim 5.

Claim 29 is directed to the LPC of claim 5 coupled to a photocleavable linker.

Claim 33 is directed to a method of solution phase biopolymer synthesis using an LPC of formula $(R^1)_p\text{-}A\text{-}(Z_t\text{-}X^1)_n$, wherein the variables are as defined therein. Claims 34-37 and 39 further define the method of claim 33.

Claim 45 is directed to the LPCs of formula



where the variables are as defined therein.

Claim 49 is directed to the LPC of claim 5 coupled to a biopolymer.

Analysis

First, applicant respectfully submits that the Office Action has raised several points in support of the written description rejection. Careful review of the arguments reveals that many of the issues raised are directed towards an enablement rejection rather than the written description rejection. Nonetheless, applicant has provided rebuttal to the arguments in the Office Action in the "Rebuttal to the Arguments in the Office Action" section of this response.

Second, applying the guidelines for a written description analysis of claims directed to a genus reveals that the written description requirement is satisfied. The analysis for compliance with the written description requirement for the claims directed to a genus is as follows:

a) does the art indicate substantial variation among the species within the genus?

b) are there a representative number of examples explicitly or implicitly disclosed in the application as determined by assessing whether the skilled artisan would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the disclosed species?

In this instance the answer to each of a) and b) is yes.

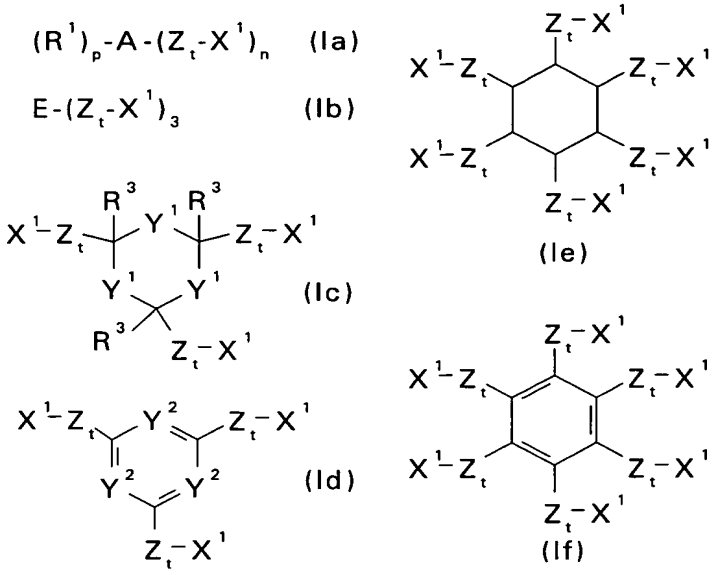
a) There is no indication in the art that there is substantial variation among members of the genus. The LPCs in instant claim 5 have the structure represented by formula (Ia) with silicon atom as a central core and substituted alkylene or phenylene units or any combination thereof as defined in claim 5, with reactive groups that are used in biopolymer synthesis at the end. Instant claims and the specification as originally filed, explicitly disclose structure of the instantly claimed LPCs. The reactive groups used in biopolymer synthesis are disclosed in the application and several references are cited

wherein the reactive groups are disclosed. The application discloses that all the LPCs within the scope of the instant claims have similar functional features. Further, as discussed in detail below those skilled in the art recognize that the instantly claimed LPCs can be prepared by slight modification of the known reaction protocols.

b) The specification explicitly describes preparation of tetrakis-{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ((DMT-dT)$_4$-PE-LPC) and tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT$_4$-PE-LPC) which represent LPCs with carbon as a central core with symmetrically substituted reactive groups that are used in biopolymer synthesis. A person of skill in the art would recognize that the instantly claimed genus of LPCs with silicon as a central core have common attributes or features possessed by the above mentioned LPCs with carbon as a central core. Therefore a skilled artisan would recognize that applicant had possession of the genus as claimed. Thus, the application complies with the written description requirement for the claims directed to a genus by meeting the requisite criterion.

Further, applicant respectfully submits that the application discloses the instantly claimed LPCs, for example, specification on page 3, line 12 through page 4, line 5 discloses:

In one embodiment, the LPCs have one of formulae (I):



where Sp is $(R^1)_p$-A, E or a cyclic group (i.e. heterocycles, carbocycles, aryls, heteroaryls, such that the resulting structure is symmetrically disposed around the center of the cyclic group) with the linked "Z_t" moieties, where t is 0 or 1. As depicted the cyclic and aromatic rings have 6 members; it is understood that fewer or higher-number membered rings may also be used, as long as the resulting structure possesses the requisite symmetry, and the number of linkages for synthesis of the biopolymers is greater than two.
In particular, A is carbon or silicon; E is nitrogen or P(O); R^1 and R^3 are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1;

The application describes all the components of the claimed LPCs. For example, Z is described on page 4, lines 5-16 as:

> Z, where t is 0 or 1, is a divalent hydrocarbon, containing one or more or mixtures of phenylene or alkylene groups, and contains a sufficient number of carbons (0, where t is 0, up to as many as 24 or more) to prevent or to reduce interactions among the chains in each biopolymer during synthesis. Preferably Z, typically containing from 1 up to 30 carbons or more, is any combination alkylene and arylene units, preferably methylene and phenylene units, preferably 1-12, more preferably 2-12, particularly 3-12, more particularly 4-12, most preferably 6-12, 7-12 or 8-

12 units, preferably selected from 1,2-, 1,3- or 1,4-, preferably 1,4-, phenylene and alkylene units, more preferably methylene units, which units may be combined in any order;

The specification on page 4, lines 16-21 discloses:

Z is a divalent hydrocarbon as described above, and is preferably any combination of 0-12, preferably 1-12, more preferably 2-12, particularly 3-12, more particularly 4-12, most preferably 6-12, 7-12 or 8-12 units in which each unit is preferably selected from 1,4-phenylene and methylene, which units may be combined in any order;

X is described in the specification on page 19, lines 29-34 as:

X^1 is any reactive group that is used in biopolymer synthesis (see, e.g., U.S. Patent No. 5,198,540, the disclosure of which is incorporated herein by reference), and is preferably halide, OH, SH, NH_2, COR^5 or $COOR^4$; n is preferably 3 or 4; R^4 is selected from hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl and heterocyclylalkyl; R^5 is halide, heteroaryl or pseudohalide;

X is further disclosed in the specification on page 19, lines 29-34, and claims 6 and 14-16.

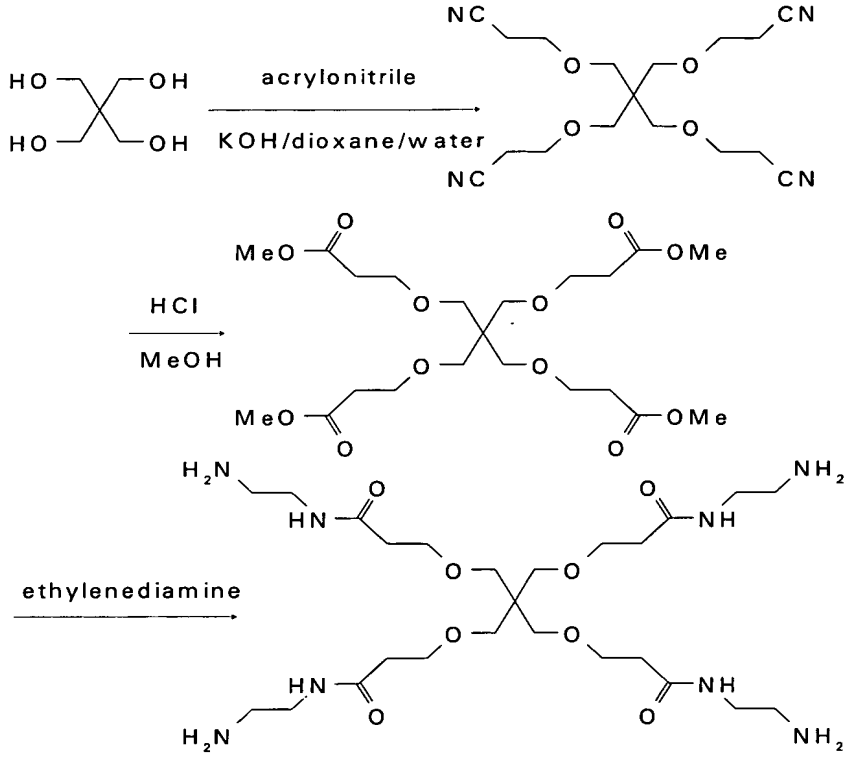
The LPC of instant claim 49 is described in claim 49 as originally filed.

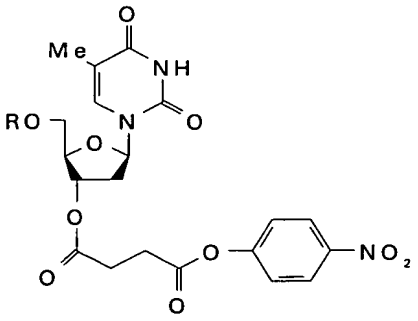
Thus, the instantly claimed LPCs are explicitly disclosed in the application as originally filed. The Examiner is reminded that possession does not mean physical possession but appreciation. It is not necessary to make and test all or any embodiments to meet the written description requirement.

Furthermore, the application demonstrates the protocol for the preparation of an exemplary LPC of formula (Ia), tetrakis-{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ($(DMT\text{-}dT)_4$-PE-LPC) and tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT_4-PE-LPC) starting from commercially available pentaerythritol as follows:

Preparation of LPCs of formula (Ia) is exemplified by the syntheses of tetrakis{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-

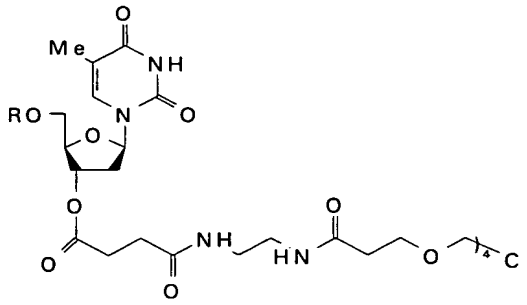
deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ((DMT-dT)$_4$-PE-LPC) and tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT$_4$-PE-LPC), shown below (see also, Examples 1 and 3). Other LPCs of formula (Ia) may be prepared by minor modification of this method.





(3'-p-nitrophenylsuccinoyl-5'-DMT-dT)

pyridine
R = 4,4'-dimethoxytrityl

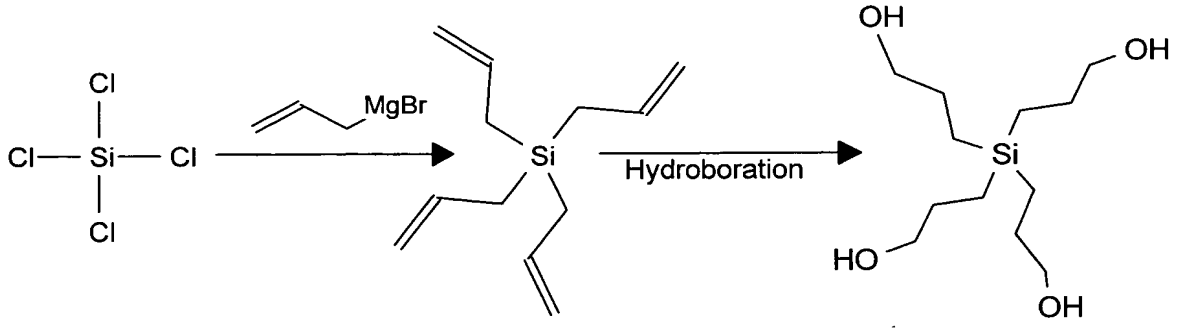


R = 4,4'-dimethoxytrityl
$\downarrow$ H^+
R = H

Treatment of pentaerythritol with acrylonitrile in the presence of KOH gave tetrakis-[(cyanoethoxy)methyl]methane. When refluxed with HCl saturated methanol under exclusion of water the nitrile reacts to form tetrakis-[((methoxy-carbonyl)ethoxy)methyl]methane. See, G.R. Newkome et al. Aldrichim. Acta **1992**, 25, 31-38; G.R. Newkome et al. Macromolecules **1991**, 24, 1443-1444 and G.R. Newkome et al. Tetrahedron: Asymmetry, **1991**, 2, 957-960. Aminolysis with ethylendiamine leads to the tetravalent amine, tetrakis-(8-amino-6-aza-2-oxa-5-oxooctyl)-methane. See, A.D. Meltzer et al. Macromolecules **1992**, 25, 4541-4548. The four primary amino functions were then acylated by the reactive p-nitrophenylester of 5'-O-dimethoxytrityl-deoxythymidine-3'-O-succinate in pyridine, leading to the highly symmetrical compound tetrakis-{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ($(DMT\text{-}dT)_4$-PE-LPC). Repeated low pressure liquid chromatography on silica gel and gel permeation chromatography (GPC) on Sephadex LH20 afforded pure material in a yield of 45%.

A skilled artisan would recognize, based on the application disclosure above, that by choosing appropriate starting materials and modification to the protocol disclosed in the application, the LPCs within the scope of the instant claims can be easily synthesized. For example, a skilled artisan would recognize that the LPCs within the scope of the instant claims, where A is silicon and Z is any combination of 0-12 units selected from 1,2-, 1,3- or 1,4-phenylene and alkylene, which units may be combined in any order, with the proviso that if Z is

methylene, then Z contains more than three methylene units and X is NH_2, COOH or OH can be prepared by starting with $Si(Cl)_4$ and performing routine sequence of reactions known in the art. Such reactions are disclosed by, for example, Lorenz *et al.* in Macromolecules **1995**, 28, 6657-6661, for the preparation of tetrakis(3-hydroxypropyl)silane from tetrachlorosilane as reproduced below:



The reaction protocols reported in the literature can be modified by a skilled artisan to arrive at the LPCs within the scope of the instant claims

Similar reactions are also reported by Hoare *et al.* in Organometallics **1997**, 16, 4167-4173.

Further, Heisteeg et al. have reported preparation of $Si(CH_2I)_4$ which can be subjected to routine sequence of rections to arrive at the LPCs within the scope of the instant claims.

Therefore a person of skill in the art would recognize that the LPCs within the scope of the instant claims wherein A is silicon; R^1 is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; and Z is any combination of 1-12 alkylene or phenylene units with the proviso that if Z is methylene, then Z contains more than three methylene units, can be prepared by choosing appropriate starting materials and slight modification to the protocol disclosed in the application. With little experimentation, a skilled artisan would be able to modify the reactions reported in the literature, to

prepare other starting materials suitable for the preparation of the LPCs of the instant claims.

It is not necessary to include in the specification that which those of skill in the art know. The specification is presumed to include all such knowledge. Thus the application as originally filed discloses the instantly claimed LPCs and describes an exemplary reaction protocol that can be modified by a skilled artisan to arrive at the LPCs of the instant claims. In light of the foregoing, the present application clearly conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was in possession of the presently claimed subject matter. Specifically, it is clear from the disclosure that the claimed LPCs can be obtained by choosing appropriate starting materials and modifying the protocol disclosed in the application.

Claims 33-37 and 39: Claims directed to method of solution phase biopolymer synthesis

Claims 33-37 and 39 are rejected under 35 U.S.C. §112 for lack of written description. The Office Action alleges that the specification does not have enough support for the claims to the method of solution phase biopolymer synthesis using the LPCs of formula (Ia). Applicant respectfully disagrees.

Relevant Law

As discussed above.

Instant claims 33-37 and 39

Independent claim 33 and dependent claims 34-37 and 39 are directed to a method of solution phase biopolymer synthesis using an LPC of formula $(R^1)_p$-A-$(Z_t$-$X^1)_n$, where A is silicon and the other variables are as defined therein. Claim 34 further defines the monomers used in the method of claim 33. Claim 35 further defines the method. Claims 36, 37 and 39 further define the LPC used in the method of the instant claims.

Analysis

A method of solution phase biopolymer synthesis with an exemplary LPC is disclosed in the application on page 8, lines 7-24; page 44, lines 4-21, and claims 33 and 48 as originally filed. The application describes an exemplary method of biopolymer synthesis in example 7 for the synthesis of d(5'-O-DMT-$G^{ib}pA^{bz}pC^{bz}pG^{ib}pG^{ib}pC^{bz}pC^{bz}pA^{bz}pG^{ib}pT)_3$-Aryl-LPC. The example describes all the steps involved in the method of biopolymer synthesis in great details. The application discloses that similar steps can applied in the method of biopolymer synthesis using LPCs within the scope of the instant claims. As discussed above, based on the application disclosure and information available in the art, a skilled artisan can choose appropriate starting materials and modifications to the protocol disclosed in the application to arrive at LPCs within the scope of formula (Ia) with silicon as a central core with little experimentation. The method for biopolymer synthesis described in detail in the application allows a skilled artisan to apply the method to LPCs within the scope of the instant claim.

Therefore, the specification provides adequate written description for the method of biopolymer synthesis using LPCs of formula (Ia) wherein A is silicon, and there is no basis to conclude that applicant was not in possession of the claimed subject matter.

REBUTTAL TO THE ARGUMENTS IN THE OFFICE ACTION

Applicant herein provides response to the specific issues raised in the Office action.

Lack of Adequate disclosure

It is alleged in the Office Action that a statement of a potential synthetic method based on the synthesis of compounds not within the general definition of the formula (Ia) as instantly claimed does not constitute a sufficient written description for **how to make LPCs** of formula (Ia) wherein A is silicon.

Applicant respectfully submits that **description of how to make the instantly claimed LPCs is irrelevant for written description requirement.** To satisfy the written description requirement, a specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, *i.e.*, whatever is now claimed. A written description requirement issue generally involves the question of whether the subject matter of a claim is supported by or conforms to the disclosure of an application as filed. As discussed above, in the instant case the LPCs of formula (Ia) are explicitly disclosed and various components thereof are described in the application on pages 3, 4, and 19, as originally filed and provide adequate written description.

Furthermore, the application discloses preparation of an exemplary LPC starting from a commercially available compound by demonstrating the steps involved in the preparation thereof. As discussed above, a skilled artisan with the information available in the art and based on his/her knowledge, can modify the disclosed reaction protocol to arrive at the LPCs of formula (Ia) as instantly claimed. Therefore, the disclosure in the application enables a person of skill in the art to make the instantly claimed LPCs. Examiner is reminded that applicant is entitled to claims that are commensurate in scope not only with what applicant has specifically exemplified, but commensurate in scope with that which one of skill in the art could obtain by virtue of that which the applicant has disclosed. It would be unfair and unduly limiting to require applicant to limit the claims to the exemplified species when the specification clearly places those of skill in the art in possession of a larger genus of the LPCs as instantly claimed. Therefore, it would be unfair, unduly limiting and contrary to the public policy upon which the U.S. patent laws are based to require applicant to limit the claims only to the exemplified species:

See, e.g., In re Goffe, 542 F.2d 801, 166 USPQ 85 (CCPA 1970):

> for the Board to limit appellant to claims involving the specific materials disclosed in the examples so that a competitor seeking to avoid infringing the claims can merely follow the disclosure and make routine substitutions "is contrary to the purpose for which the patent system exists - to promote progress in the useful arts".
>
> The public purpose on which the patent law rests requires the granting of claims commensurate in scope with the invention disclosed. This requires as much the granting of broad claims on broad inventions as it does the granting of more specific claims on more specific inventions" In re Sus and Schafer, 49 CCPA 1301, 306 F.2d 494, 134 USPQ 301, at 304.

To require applicant to limit the claims to only the exemplified species would permit those of skill in the art to practice what is disclosed in the application, but avoid infringing such limited claims. One of skill in the art could readily modify the exemplified LPCs disclosed in the application as taught in the specification. The first paragraph of §112 requires only that the disclosure be sufficient to teach one of skill in the art how to make and use the claimed subject matter without undue experimentation. As discussed above, the specification discloses the LPCs and describes various components thereof in detail. Based upon the disclosure those skilled in the art can make and use the LPCs as claimed.

Further, a patentee not only is entitled to narrow claims particularly directed to a specific embodiment, but also to broad claims that define an invention without a reference to specific instrumentalities. *Smith v. Snow*, 294 U.S. 1, 11, 24 USPQ 26, 30 (1935). As discussed above, applicant has described the LPCs and provided an exemplary protocol to make certain LPCs. Based on this disclosure, a person of skill in the art can make LPCs within the scope of instant claims.

As discussed above, the instant application discloses preparation of tetrakis methyl LPCs. A skilled artisan, with little experimentation could carry out routine sequence of reactions known in the art using appropriate starting

materials, for example, tetrachlorosilane, to arrive at the LPCs of instant claims. Furthermore, it is not necessary to make and test all or any embodiments to meet written description requirement. Therefore, applicant respectfully submits that based on the specification disclosure, wherein an exemplary synthesis of LPCs based on tetrasubstituted methane is described, a person of skill in the art, using his/her own knowledge and the information in the art, would be able to synthesize the instantly claimed LPCs with silicon as a core.

Predictability in the art

The Office Action alleges that there is no predictability established in the art with respect to synthesizing a silicon atom substituted with an alkyl, phenyl, alkylphenyl, or phenylalkyl based on the synthesis of methane tetra-substituted with 8-amino-6-aza-2-oxa-5-oxooctyl.

As discussed above, the synthesis of instantly claimed LPCs can be achieved by using appropriate starting materials and by modifications to the protocol disclosed in the application. For example, tetrasubstituted silanes reported in the art or can be prepared by a skilled artisan with little experimentation from the knowledge available in the art, can be used for the preparation of the instantly claimed LPCs using routine modifications to the protocol disclosed in the application. As evidenced by the articles discussed above, such reactions have well established predictability in the art. The question of predictability in the art for synthesizing a silicon atom substituted with an alkyl, phenyl, alkylphenyl, or phenylalkyl based on the synthesis of methane tetra-substituted with 8-amino-6-aza-2-oxa-5-oxooctyl is irrelevant because a person of skill in the art would recognize that the instantly claimed LPCs can be made with appropriate starting materials and modifications to the protocol disclosed in the application. As discussed above, tetrasubstitued silanes reported in the literature can be easily converted to the instantly claimed silicon based LPCs with routine sequence of reactions.

Methodology for carbon-carbon bond formation

The Office Action alleges that to provide adequate support for the breadth of the claims, applicant would have to establish that the methodology for carbon-carbon bond formation is the same for attaching an alkyl or phenyl group to a silicon based compound as for attaching an amide to methane. The Office Action notes that the data presented shows the synthesis of methane substituted with an amide or diamide.

As discussed above, a skilled artisan, based the information available in the art, would recognize that various substituted silanes can be used as starting materials to arrive at instantly claimed LPCs with little experimentation. Therefore, there is no need to establish that the methodology for carbon-carbon bond formation is the same for attaching an alkyl or phenyl group to a silicon based compound as for attaching an amide to methane.

Data presented in the application

The Office Action alleges that the data is not seen to be adequately correlative for the elected species of a silicon based compound substituted with an alkyl or phenyl group as broadly claimed. The Office Action further urges that an adequate representation of species requires that the species that are expressly described be representative of the entire genus and what constitutes a "representative number" is an inverse function of the predictability of the art. The Office Action further alleges that a skilled artisan would not recognize that a compound capable of being synthesized via standard carbonyl chemistry would be representative of compounds incapable of being synthesized in a similar manner. It is further urged that a skilled artisan would not recognize that a diamide compound linked to a nucleoside would be representative in function to the silicon-based alkyl, phenyl, alkylphenyl, or phenylalkyl compound as brodly claimed.

As discussed above, the application discloses synthesis of tetrakis-{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-2-

oxa-5,10,13-trioxotridecyl}methane ((DMT-dT)$_4$-PE-LPC) and tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT$_4$-PE-LPC) starting from commercially available pentaerythritol. Further, the LPCs of instant claims are explicitly disclosed in the application. Applicant respectfully submits that the reactions illustrated in the application demonstrating the preparation an exemplary LPC and its use in the biopolymer synthesis can be easily extended by a skilled artisan for the preparation of LPCs within the scope of the instant claims based on the application disclosure and the information available in the art. Such reactions involve routine chemistry which has well established predictability in the art. Furthermore, there is no need to disclose any examples in the application to satisfy written description requirement and the applicant is entitled to claim routine modifications to the specific examples disclosed.

Compounds of instant claims

The Office Action concludes that there is no data to support applicant's claim that at the time of filing, the compounds of the instant claims were **made and used** by minor modification to the protocol developed for the diamide compounds.

Applicant respectfully submits that the Office Action is once again raising the issue of enablement in the written description rejection. The question of "make and use" is irrelevant in written description rejection. As stated in the Office Action, a written description analysis involves:

1) field of the invention and predictability of the art,
2) breadth of the claims, and
3) possession of the claimed invention at the time of filing for each claimed species/genus.

None of these factors require "make and use" aspect of the claimed subject matter. The Examiner is reminded that there is no requirement to prepare any or all embodiments of the claimed LPCs to satisfy written

description requirement and examples are not required to satisfy written description. The application as originally filed, discloses the instantly claimed LPCs and describes all the components thereof. Further, possession does not mean physical possession but appreciation. In light of the discussion presented above, the present application clearly conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was in possession of the presently claimed subject matter. Specifically, it is clear from the disclosure that the claimed LPCs can be obtained by choosing appropriate starting materials and modifying the protocol disclosed in the application.

Use of instantly claimed LPCs

Applicant respectfully submits that the application discloses the use of LPCs of formula (Ia) in the method for biopolymer synthesis, for example in the specification on page 44 as originally filed. Example 7 demonstrates the steps involved in the synthesis of d(5'-O-DMT-$G^{ib}pA^{bz}pC^{bz}pG^{ib}pG^{ib}pC^{bz}pC^{bz}pA^{bz}pG^{ib}pT)_3$-Aryl-LPC, which can be applied to the instantly claimed LPCs with silicon as a central core. As discussed above, based on the application disclosure and information available in the art, a skilled artisan can further prepare other LPCs of formula (Ia) wherein A is silicon, for use in the instantly claimed method for biopolymer synthesis.

REJECTION OF CLAIMS 12-14, 16, 17 AND 20 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 5-7, 11-13, 29, 33-37, 39, 45 and 49 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and disctictly claim the subject matter. Applicant respectfully traverses this rejection.

"any rective group"

Independent claims 5, 33 and 45 are rejected for reciting the term "any reactive group", which is alleged to be indefinite. The Office Action alleges that in the absence of particular moieties that would be construed as reactive groups or distict language to describe the structural features or the chemical names of the reactive groups for use in the instant compounds, the identity of such groups would be difficult to describe. Applicant disagrees.

Applicant respectfully submits that the specification describes the reactive group as groups used in effecting synthesis of biopolymers. Examples of rective groups for use in the instant claims are provided in the specification, see, *e.g.*, page 17, lines 10-24, which recite:

> Examples of the reactive group X^1 which are customary in nucleotide chemistry are described in Liebigs Ann. Chem. **1978**, 839-853 and in Nucleic Acids Research, Symposium Series No. 7, **1980**, 39-59. Typical examples are, inter alia, the following:
> 1. Acid halides, in particular acid chlorides and acid bromides;
> 2. Carboxylic acid groups, which can react with 5'-OH groups, for example in the presence of condensing agents; they can also be converted into activated trityl chloride derivatives according to the following equation:
>
> $$-COOH + Y-C_6H_4(C_6H_5)_2C-Cl \; - - > \; -CO-Y'-C_6H_4(C_6H_5)_2C-Cl,$$
>
> wherein Y = OH, SH or NH_2; and Y' = O, S or NH;
> 3. Activated ester functions of the general formula —COOR'; and
> 4. OH, SH and NH_2 groups.

Therefore, the term "any reactive group" does not render claims 5, 33 and 45 indefinite.

"pseudohalide"

Claims 6 and 39 are rejected for reciting the term "pseudohalide" which is alleged to be indefinite. The Office Action alleges that in the absence of particular moieties that would be construed as pseudohalides or distict language to describe the structural features or the chemical names of the pseudohalides

for use in the instant compounds, the identity of such groups would be difficult to describe.

Applicant respectfully submits that "pseudohalides" are defined and exemplified in the specification, see, *e.g.*, page 12, lines 25-29, which recite:

> As used herein, pseudohalides are compounds that behave substantially similar to halides. Such compounds can be used in the same manner and treated in the same manner as halides (X^-, in which X is a halogen, such as Cl or Br). Pseudohalides include, but are not limited to cyanide, cyanate, thiocyanate, selenocyanate, trifluoromethyl and azide.

Therefore, the term "pseudohalide" does not render claims 6 and 39 indefinite.

Applicant respectfully requests reconsideration and withdrawal of this rejection.

* * *

In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	KÖSTER *et al.*
Serial No.:	09/067,337
Confirmation No.:	9981
Filed:	April 27, 1998
For:	*SOLUTION PHASE BIOPOLYMER SYNTHESIS*
Art Unit:	1623
Examiner:	Wilson, J.

ATTACHMENTS TO RESPONSE TO OFFICE ACTION

The following attachment is provided:

(1) Marked up claims 5, 12, 13 and 33 in accord with 37 CFR §1.121.

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Art Unit: 1623

Examiner: Wilson, J.

MARKED UP CLAIMS (37 CFR §1.121)

IN THE CLAIMS:

Please amend claims 5, 12, 13 and 33 as follows:

5. (Amended Three times) A liquid phase carrier (LPC) that has formula (Ia):

$(R^1)_p$-A-$(Z\text{-}X^1)_n$ (Ia)

wherein: A is silicon; R^1 is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; Z is any combination of 1-12 units selected from 1,2-, 1,3- or 1,4-phenylene and alkylene units, which units may be combined in any order; [t is 1]; X^1 is any reactive group which can be used in biopolymer synthesis; n is 3 or 4; with the proviso that if Z is methylene, then Z contains more than three methylene units; R^1, X^1, and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkyl-aminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,

arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl.

12. (Amended Twice) The LPC of claim 5, wherein Z is any combination of 1-12 units selected from 1,4-phenylene and methylene, which units may be combined in any order, with the proviso that if Z is methylene, then Z contains more than three methylene units.

13. (Amended Twice) The LPC of claim 5, wherein Z is C_{1-12} alkylene, with the proviso that if Z is methylene, then Z contains more than three methylene units.

33. (Amended Three times) A method of solution phase biopolymer synthesis, comprising the steps of:

(a) reacting an LPC of formula $(R^1)_p$-A-$(Z_t$-$X^1)_n$ with a first monomer N^1;

(b) separating and purifying the product of step (a) to afford a compound of formula $(R^1)_p$-A-$(Z_t$-X^1-$N^1)_n$;

(c) reacting the product of step (b) with a second monomer N^2, a dimer N^2-N^3 or a trimer N^2-N^3-N^4; and

(d) repeating steps (b) and (c) to produce an LPC-bound biopolymer of formula $(R^1)_p$-A-$(Z_t$-X^1-N^1-N^2-...-$N^m)_n$, where m is 3 to 100, wherein:
A is silicon; R^1 is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; Z is any combination of 0-12 units selected from 1,2-, 1,3- or 1,4-phenylene and alkylene, which units may be combined in any order; t is 0 or 1; X^1 is any reactive group which can be used in biopolymer synthesis; n is 3 or 4; with the proviso that if Z is methylene, then

Z contains more than three methylene units; R^1, X^1, and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyano, isothiocyano, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl; and

N^1, N^2, N^3...N^m are biopolymer monomers; and

the dimers and trimers comprise the monomers.